CLAIMS

1. A DNA sequence encoding a B1 protein, isoforms, fragments, or analogs thereof, said B1 protein, isoforms, fragments or analogs thereof being capable of interacting with intracellular mediators or modulators of inflammation, cell death or cell survival pathways directly or indirectly, said B1 protein, isoforms, fragments or analogs being intracellular modulators of said intracellular inflammation, cell death and/or cell survival pathways.

2. A DNA sequence according to claim 1 selected from the group consisting of:

(a) a cDNA sequence derived from the coding region of a native B1 protein;

(b) a fragment of a sequence of (a) which encodes a biologically active protein capable of modulating the inflammation, cell death or cell survival pathways;

(c) a DNA sequence capable of hybridization to a sequence of (a) or (b) under moderately stringent conditions and which encodes a biologically active B1 protein, analog or fragment capable of modulating the intracellular inflammation, death or cell survival pathways;

(d) a DNA sequence which is degenerate as a result of the genetic code to the DNA sequences defined in (a)-(c) and which encodes a biologically active B1 protein, analog or fragment capable of modulating the inflammation, cell death or cell survival pathways.

3. A DNA sequence according to claim 1 or claim 2 comprising at least part of the sequence depicted in Fig. 3 and encoding at least one active B1 protein, isoform, analog or fragment.

4. A DNA sequence according to claim 3 encoding a B1 protein, isoform, analog or fragment having at least part of the amino acid sequence depicted in Fig. 3.

5. A vector comprising a DNA sequence according to any one of claims 1-4.

6. A vector according to claim 5 capable of being expressed in a eukaryotic host cell.

7. A vector according to claim 5 capable of being expressed in a prokaryotic host cell.

8. Transformed eukaryotic or prokaryotic host cells containing a vector according to any one of claims 5-7.

9. A B1 protein, isoforms, fragments, functional analogs and derivatives thereof, encoded by a DNA sequence according to any one of claims 1-4, said protein, isoforms, fragments, analogs and derivatives thereof being capable of modulating the intracellular inflammation, cell death or cell survival pathways, directly or indirectly by association with other intracellular modulators or mediators of these pathways.

10. A B1 protein, isoform, fragment, analogs and derivatives thereof according to claim 9, wherein said protein, isoform, analogs, fragments and derivatives have at least part of the amino acid sequence depicted in Fig. 3.

11. A method for producing a B1 protein, isoform, fragment, analog or derivative thereof according to claim 9 or 10, which comprises growing a transformed host cell according to claim 8 under conditions suitable for the expression of said protein, isoform, fragment, analog or derivative thereof, effecting post-translational modification, as necessary, for obtaining said protein, isoform, fragment, analog or derivative thereof, and isolating said expressed protein, isoform, fragment, analog or derivative.

12. Antibodies or active fragments or derivatives thereof, specific for the B1 protein, isoform, analog, fragment or derivative thereof according to claim 9 or 10.

13. A method for the modulation or mediation in cells of the activity of inflammation, cell death or cell survival pathways or any other intracellular signaling activity modulated or mediated directly or indirectly by B1 or by other molecules to which a B1 protein, isoform, analog, fragment or derivative thereof according to claim 9 or 10 binds or otherwise interacts, directly or indirectly, said method comprising treating said cells by introducing into said cells one or more of said B1 protein, isoform, analog, fragment or derivative thereof in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more B1 protein, isoform, analog, fragment or derivative thereof in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

14. A method according to claim 13, wherein said treating of cells comprises introducing into said cells a DNA sequence encoding said B1 protein, isoform, fragment, analog or derivative in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

15. A method according to claim 13 or 14 wherein said treating of said cells is by transfection of said cells with a recombinant animal virus vector comprising the steps of:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand) that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding a protein selected from said B1 protein, isoforms, analogs, fragments and derivatives according to claim 9 or claim 10, that when expressed in said cells is capable of modulating/mediating the activity of the inflammation, cell death or cell survival pathways directly or indirectly, or any other intracellular signaling activity modulated/mediated by other intracellular molecules with which said B1 protein, isoforms, analogs, fragments and derivatives interact directly or indirectly; and

(b) infecting said cells with said vector of (a).

16. A method for modulating the inflammation, cell death or cell survival pathways in cells which are modulated directly or indirectly by B1, comprising treating said cells with antibodies or active fragments or derivatives thereof, according to claim 12, said treating being by application of a suitable composition containing said antibodies, active fragments or derivatives thereof to said cells, wherein when the B1 protein or portions thereof of said cells are exposed on the extracellular surface, said composition is formulated for extracellular application, and when said B1 proteins are intracellular said composition is formulated for intracellular application.

17. A method for modulating the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by B1, comprising treating said cells with an oligonucleotide sequence encoding an antisense sequence for at least part of the DNA sequence encoding a B1 protein according to any one of claims 1-4, said oligonucleotide sequence being capable of blocking the expression of the B1 protein.

18. A method according to claim 17 wherein said oligonucleotide sequence is introduced to said cells via a virus of claim 15 wherein said second sequence of said virus encodes said oligonucleotide sequence.

19. A method for modulating the inflammation, cell death or cell survival or other pathways in which cells are modulated directly or indirectly by B1, comprising applying the ribozyme procedure in which a vector encoding a ribozyme sequence capable of interacting with a cellular mRNA sequence encoding a B1 protein according to claim 9 or

10, is introduced into said cells in a form that permits expression of said ribozyme sequence in said cells, and wherein when said ribozyme sequence is expressed in said cells it interacts with said cellular mRNA sequence and cleaves said mRNA sequence resulting in the inhibition of expression of said B1 protein in said cells.

20. A method for isolating and identifying proteins, according to claim 9 or 10, having homology with or being capable of direct or indirect interactions with any proteins having a prodomain or caspase recruiting domain (CARD), or other proteins or enzymes involved in intracellular signaling, via the kinase or intermediate domains present in said proteins according to claim 9 or 10, comprising applying the yeast two-hybrid procedure in which a sequence encoding said protein with said CARD, kinase, and intermediate domains, or at least one of these domains, is carried by one hybrid vector and a sequence from a cDNA or genomic DNA library is carried by the second hybrid vector, the vectors then being used to transform yeast host cells and the positive transformed cells being isolated, followed by extraction of the said second hybrid vector to obtain a sequence encoding a protein which binds to said CARD-, kinase-, and/or intermediate domain-containing protein.

21. A method according to any one of claims 13-20 wherein said protein is at least one of the B1 isoforms, analogs, fragments and derivatives thereof.

22. A pharmaceutical composition for the modulation of the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by B1, comprising, as active ingredient, at least one B1 protein, according to claim 9 or 10, its biologically active fragments, analogs, derivatives or mixtures thereof.

23. A pharmaceutical composition for the modulation of inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by B1, comprising, as active ingredient, a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor and encoding at least one B1 protein, isoform, active fragments or analogs, according to claim 9 or 10.

24. A pharmaceutical composition for modulating the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by B1, comprising as active ingredient, an oligonucleotide sequence encoding an anti-sense sequence of the B1 protein mRNA sequence, according to any one of claims 1-4.

25. A pharmaceutical composition is one for the prevention or treatment of a pathological condition associated with the regulation of apoptosis by one or more molecules to which a B1 protein, according to claim 9 or 10, binds directly or indirectly, said composition comprising an effective amount of a B1 protein or a DNA molecule coding therefor, or a molecule capable of disrupting the direct or indirect interaction of said B1 protein with one or more molecules to which a B1 protein binds or with which it interacts.

26. A pharmaceutical composition for the prevention or treatment of a pathological condition associated with the regulation of apoptosis by one or more molecules to which a B1 protein, according to claim 9 or 10, binds directly or indirectly, said composition comprising an effective amount of a B1 protein, isoform, fragment, analog or derivative thereof, or a DNA molecule coding therefor, or a molecule capable of disrupting the direct or indirect interaction of said B1 protein, isoform, fragment, analog or derivative thereof with one or more molecules to which said B1 protein, isoform, fragment, analog or derivative binds.

27. A pharmaceutical composition is one for the prevention or treatment of a pathological condition associated with the regulation of apoptosis by one or more molecules to which the B1 protein, according to claim 9 or 10, binds directly or indirectly, said composition comprising a molecule capable of interfering with the protein kinase activity of B1.

28. A method for the prevention or treatment of a pathological condition associated with the regulation of apoptosis by one or more molecules to which a B1 protein, according to claim 9 or 10, binds directly or indirectly, said method comprising administering to a patient in need an effective amount of a protein or isoform, fragment, analog and derivative thereof or a mixture of any thereof, according to claim 9 or 10, or a DNA molecule coding therefor, or a molecule capable of disrupting the direct or indirect interaction of said B1 protein or isoform, fragment, analog and derivative thereof or a mixture of any thereof, according to claim 9 or 10, with one or more molecules to which said B1 protein or isoform, fragment, analog and derivative thereof or a mixture of any thereof, according to claim 9 or 10, binds directly or indirectly.

29. A method of modulating apoptopic processes or programmed cell death processes (cell death pathways) in which the B1 protein is involved directly or indirectly,

comprising treating said cells with one or more B1 proteins, isoforms, analogs, fragments or derivatives, according to claim 9 or 10; wherein said treating of said cells comprises introducing into said cells said one or more B1 proteins, isoforms, analogs, fragments or derivatives in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more B1 proteins, isoforms, analogs, fragments or derivatives in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

30. A method of modulating cell survival processes in which the B1 protein is involved directly or indirectly and which include the modulation of cell survival, comprising treating said cells with one or more B1 proteins, isoforms, analogs, fragments or derivatives, according to claim 9 or 10, wherein said treating of cells comprises introducing into said cells said one or more B1 proteins, isoforms, analogs, fragments or derivatives in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more B1 proteins, isoforms, analogs, fragments or derivatives in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

31. A method for screening of a ligand capable of binding to a B1 protein according to claim 9 or 10, comprising contacting an affinity chromatography matrix to which said protein is attached with a cell extract whereby the ligand is bound to said matrix, and eluting, isolating and analyzing said ligand.

32. A method for screening of a DNA sequence coding for a ligand capable of binding to a B1 protein according to claim 9 or 10, comprising applying the yeast two-hybrid procedure in which a sequence encoding said B1 protein is carried by one hybrid vector and sequences from a cDNA or genomic DNA library are carried by the second hybrid vector, transforming yeast host cells with said vectors, isolating the positively transformed cells, and extracting said second hybrid vector to obtain a sequence encoding said ligand

33. A method for identifying and producing a ligand capable of modulating the cellular activity modulated/mediated by B1 comprising :

a) screening for a ligand capable of binding to a polypeptide comprising at least a portion of B1 having at least some of the amino acid residues of B1 depicted in Fig. 3, which include essentially all of the prodomain (or CARD) of B1;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

34. A method for identifying and producing a ligand capable of modulating the cellular activity modulated or mediated by a B1 protein according to claim 9 or 10- comprising :

a) screening for a ligand capable of binding to a polypeptide comprising at least the carboxy terminal portion of the B1 sequence depicted in Fig. 3 including the prodomain (CARD);

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

35. A method for identifying and producing a ligand capable of modulating the cellular activity modulated/mediated by B1 comprising :

a) screening for a ligand capable of binding to at least the N-terminal portion of the B1 sequence depicted in Fig. 3 including substantially all of the kinase domain of B1;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known intracellular modulatory proteins, found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

36. A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated/mediated by B1, comprising :

a) screening for a molecule capable of modulating activities modulated/mediated by B1;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.

37. A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated/mediated by a protein according to claim 9 ~~or 10~~, comprising :

a) screening for a molecule capable of modulating activities modulated/mediated by a protein according to claim 9 ~~or 10~~;

b) identifying and characterizing said molecule; and

c) producing said molecule in substantially isolated and purified form.

38. A fragment according to claim 9 being a peptide.

39. A method of modulating cell-death, cell survival and/or inflammation comprising treating cells with a molecule which is capable of interacting with the E-subunit of V-ATPase.